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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,195	06/30/2005	Patricia Salvati	108942-00006	7746

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EXAMINER	
JAVANMARD, SAHAR	

ART UNIT	PAPER NUMBER
1617	

NOTIFICATION DATE	DELIVERY MODE
12/14/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/541,195	SALVATI ET AL.	
	Examiner	Art Unit	
	SAHAR JAVANMARD	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 12-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 12-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *30 June 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

This Office Action is in response to the Response to Restriction Requirement filed on November 19, 2007. Claims 1-10 and 12-14 are pending in this Application. The applicant has amended the "use" claims language to "methods of use". The instant claims are examined on the merits herein.

Election/Restriction

In response to the Office Action mailed on October 22, 2007, Applicants provisionally elect Group II. Applicant's election with traverse of Group II in reply on November 11, 2007 is acknowledged.

The traversal is on the grounds that Applicants submit that the Restriction Requirement is rendered moot, as all of the claims are now directed to the invention of Group II, which is "a method for the treatment of head pain conditions in a mammal in need thereof comprising administering to the mammal a therapeutically effective dose of at least one a-aminoamide of formula (I)." Applicants submit that all pending claims, claims 1-10 and 12-14 are directed to the invention of Group II.

Further, the Applicants traverse the Election of Species Requirement asserted.

The Examiner has fully considered the traversal and finds the arguments persuasive. Therefore the restriction requirement and Election of Species have been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 and 12-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for compounds of formula I wherein R is a phenyl ring, unsubstituted or substituted by one or two substituents independently selected from halogen, hydroxy, C1-C4 alkyl, C1-C3 alkoxy and trifluoromethyl, the specification does not reasonably provide enablement for wherein R is a furyl, thienyl, or pyridyl ring. Thus, the variable R is very broad as cited in claims 1-10 and 12-14.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The specification does not provide sufficient information that compounds of formula I wherein R is a furyl, thienyl, or pyridyl ring are capable of treating head pain conditions.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1). The Nature of the Invention:

All of the rejected claims are drawn to an invention which pertains to a method of treating head pain conditions with the administration of compounds of Formula I wherein R is a furyl, thienyl, or pyridyl ring as described in claims 1-10 and 12-14.
The nature of the invention is complex in that it encompasses the treatment of said ailments using a wide array of compounds encompassed by the variable R wherein the variable includes furyl, thienyl, or pyridyl rings.

(2). Breadth of the Claims:

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass methods of treating head pain conditions with the administration of compounds of Formula I wherein R is a furyl, thienyl, or pyridyl ring. There are countless possible compounds by defining R as such for the treatments claimed. The claims are therefore much broader than the enabling disclosure.

(3). Guidance of the Specification:

The guidance given by the specification as to how effective the disclosed alpha-aminoamide compounds are at treating the desired ailments is very limited. On page 15 of the specification there can be found only a few examples of the compounds tested, namely (S)-(+)-2-[4-(3-fluorobenzyloxy)benzylamino]- propanamide (internal code and hereinafter NW-1015), (S)-(+)-2- [4-(2-fluorobenzyloxy)benzylamino]-propanamide (internal code and hereinafter NW-1029) and (S)-(+)-2-[4-(3-chlorobenzyloxy)benzylamino]-propanamide (internal code and hereinafter NW-1039), 2-(4-(2- fluorobenzyloxy)benzylamino)-2-methyl-propanamide (internal code and hereinafter NWI050), and 2-(4-(4- fluorobenzyloxy)benzylamino)-2-methyl-propanamide (internal code and hereinafter NWI055). This is nowhere near the coverage of compounds encompassed by the breadth of the claims.

(4). Working Examples:

Applicant provides in vivo testing of the five compounds mentioned above (i.e. NW-1015, NW-1029, NW-1039, NW-1050, NW-1055) for their ability to treat migraine headaches.

(5). State of the Art:

A new era in antimigraine drugs began in 1973 with efforts to synthesize a more selective 5-HT_1 agonist. Prior research had indicated that serotonin 5-HT (a potent vasoconstrictor and a pain modulator) was a factor in the generation of migraine.

Triptan antimigraine agents are serotonergic agonists that act selectively. They cause vasoconstriction by affecting serotonin (5-HT_{1B}) receptors in human intracranial arteries and inhibit nociceptive transmission by their effect on 5-HT_{1D} receptors on peripheral trigeminal sensory nerve terminals in the meninges and central terminal in brain stem sensory nuclei. Those complementary sites of action are the basis of the clinical effectiveness of those 2 types of agonists in treating migraine pain and its associated symptoms (Gallagher, *American Journal of Managed Care*).

(6). Nature and predictability of the invention

The nature of the invention is directed towards medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F. 2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(7). The Quantity of Experimentation Necessary:

In order to practice the claimed invention, one of skill in the art would have to first envision a combination of an appropriate pharmaceutical carrier, a dosage for each compound as encompassed by Formula I wherein R is a furyl, thienyl, or pyridyl ring, the duration of treatment, route of treatment, the bioavailability, etc. and, in the case of human treatment, an appropriate animal model system for one of the claimed compounds. One would then need to test the combination in the model system to

determine whether or not the combination is effective for treating head pain conditions. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding head pain treatment with any compound of Formula I, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to treat head pain conditions by the administration of one of the compounds of Formula I wherein R is a furyl, thienyl, or pyridyl ring as set forth in the claims.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, treating head pain conditions by administering the various compounds of Formula I wherein R is a furyl, thienyl, or pyridyl ring of the claims is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6-10, 12, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Pevarello et al. (WO 99/35125).

Pevarello teaches compounds of formula I (page 2, line 2- page 5, line 26) as therapeutic agents used for treating pain associated with damage or permanent alteration of the peripheral or central nervous systems such peripheral neuropathies e.g. trigeminal and post-therapeutic neuralgia, diabetic neuropathy, glossopharyngeal neuralgia, radiculopathy, neuropathy secondary to metastatic infiltration, adiposis dolorosa and burn pain and central pain conditions such as those following stroke, thalamic lesions and multiple sclerosis (page 6, lines 13-22). Thus the limitations of claims 1-4 and 7-10 are met.

Claim 6 recites treating head pain conditions involving cerebral vasodilation mechanisms, is not of patentable weight. Pain is pain, no matter the mechanism by which it occurs, thus meeting the limitations of claim 6.

Pevarello further discloses a dosing regimen where the compounds of interest, specifically (S)-2-[4-(3-fluorobenzyloxy)benzylamino]-propanamide, were administered in doses of 7.5, 15.0, 30.0 and 60.0 mg/kg (page 12, lines 20-26), meeting the limitations of claims 12 and 13.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pevarello et al. as applied to claims 1-4, 6-10, 12, and 13 above.

Pevarello is discussed above.

Pevarello teaches teaches (S)-2-[4-(3-fluorobenzyloxy)benzylamino]-propanamide, however does not specifically teach the (+) optical isomer as recited in claim 5.

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have known that the (S) racemate as taught by Pevarello is a mixture of (+) and (-) isomers.

The fundamentals of optical activity and stereoisomerism are well known to persons having ordinary skill in the art. A person having ordinary skill in the art would have known how to resolve the racemic mixture and would have been motivated to do so with the reasonable expectation of achieving enantiomers having substantially different pharmacological activity. It appears as though applicant has determined experimentally what a person of ordinary skill in the art would have expected, namely, that the racemic mixture of the prior art may be separate (+) and (-) enantiomers possessing substantial different pharmacological activity. This is an expected result. It is well established that expected beneficial results are evidence of obviousness of a claimed invention just as unexpected beneficial results are evidence of unobviousness. *In re Skoll*, 523 F. 2d 1392, 187 U.S.P.Q. 481 (C.C.P.A. 1975); *In re Skoner*, 517 F. 2d 947, 186 U.S.P.Q. 80 (C.C.P.A. 1975); *In re Gershon*, 372 F. 2d 535, 152 U.S.P.Q. 602 (C.C.P.A. 1967);

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pevarello et al. as applied to claims 1-10, 12, and 13 above and further in view of Lan et al. (WO 99/26614A1).

Pevarello is discussed above.

Pevarello does not teach a dose range from 0.5-5 mg/kg.

Lan discloses substituted 2-aminoacetamides represented by formulas I and II for the treatment of a number of ailments including migraine headaches (page 7, line 22-page 8, line 3). Further, a dosage regimen for said compounds ranging from 0.0025 to 50 mg/kg is taught (page 24, lines 12-22).

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have employed the 2-aminoacetamides compounds taught by Pevarello in the dose ranges taught by Lan.

The dosage regimen of the compounds of interest is deemed to be a manipulatable parameter practiced by a person skilled in the art to obtain the best possible range.

Conclusion

Claims 1-10 and 12-14 are not allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sahar Javanmard whose telephone number is (571) 270-3280. The examiner can normally be reached on 8 AM-5 PM MON-FRI (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

SJ

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER